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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/790,914
Filing Date: March 02, 2004
Appellant(s): QI ET AL.

QI ET AL.

For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed December 12, 2007 appealing from the Office action mailed March 23, 2007.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of invention contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The Appellant's statement of the issues in the brief is correct.

Upon further review and consideration, the rejection of claims 9-10 under 35 U.S.C. 102 (a) as anticipated by Loyola-Rodriguez et al *(J. Gen. Microbiol., 138:269-274, 1992)* is withdrawn.

(7) Claims Appendix

Appellant's copy of the appealed claims contained in the appendix is correct.

(8) *Evidence Relied Upon*

O'Brien et al *(American Family Physicians, May 1, 2003, 67, 9).*

Koch et al *(Vaccine 22, 2004, pages 822-830).*

Ooshima et al *(Microbiol. Immunol., Vol. 29 (12), 1163-1173, 1985).*

Ikeda et al *(Infection and Immunity, 1982, Vol. 35, No. 3, p. 861-868).*

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

I. Claims 9-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The claimed invention is directed to methods of treating and preventing gram-positive infections in a subject comprising administering to the subject an effective amount of a purified and isolated peptide having the amino acid sequence as set forth in SEQ ID NO 2 or a pharmaceutically acceptable salt, ester or prodrug thereof.

The claimed invention encompasses a method of treating or preventing all gram-positive bacterial infections.

Pages 22-28 of the instant specification describes the isolation and purification of mutacin I. However, the specification fails to disclose methods of treating or preventing any or all gram-positive infections in a subject. Although the specification contemplates the broad spectrum use of mutacin I can be used to treat against a variety of microorganism, the specification fails to teach or disclose data that demonstrates that the amino acid sequence as set forth in SEQ ID NO: 2 can used to provide treat or protect against infections caused by any or all gram positive microorganisms. There is no disclosure of subjects that have been immunized using the claimed method nor is there a disclosure of challenge studies that have been conducted to establish that the amino acid sequence used in the claimed method has the ability to provide treatment or protection against any or all gram-positive infections.

The claimed method encompasses treating and preventing infections caused by all gram-positive bacteria. This includes gram-positive bacteria such as *Bacillus anthracis* and *Clostridium botulinum*. O'Brien et al *(American Family Physicians, May 1, 2003, 67, 9)* teach microbes that are used in bioterrorism include *Bacillus anthracis* and *Clostridium botulinum* (page 1928). O'Brien et al teach that familiarity with infectious

agents of highest priority can expedite diagnosis and initial management and lead to a successful public health response to a bioterrorist attack (see the Abstract). O'Brien et al has taught that gram-negative bacteria can be quite difficult to diagnosis as well as manage infections caused by these organisms.

The specification has not shown that mutacin I can be used to treat or prevent infections caused by all gram-positive microorganisms. The claimed invention broadly encompasses any infection or disease caused by any gram-positive microorganism.

The claims also broadly encompass all species within the of *Streptococcus, Staphylococcus* or *Enterococcus* genera. Koch et al (*Vaccine 22, 2004, pages 822-830)* teach that the emergence of resistance against multiple antibiotics and the increasing frequency with which *Enterococcus faecalis* and *Enterococcus faecium* are isolated from hospitalization patients underscore the necessity for a better understanding of the virulence mechanisms of this pathogen and the development of alternatives to current antibiotic treatments (see the Abstract). Koch et al teach that enterococci are intrinsically not as virulent as other gram-positive organisms such as *Staphylococcus aureus,* pneumococci or group A streptococci which makes the study of their pathogenicity more difficult (page 822). Koch et al teach that the rapid increase in enterococcal strains resistant to vancomycin and other antibiotics and their ability to pass this trait on to other pathogens, i.e. *Staphylococcus aureus,* indicates an urgent and expanding clinical problem (page 822).

The above mentioned infections/diseases are only a few of the microorganisms that are encompassed by the claimed invention and represent a small subset of the

many diseases that exist that have no vaccine that is effective in treating and/or preventing such infectious diseases. The specification has not shown that mutacin I can be used to treat or prevent infections caused by any gram-positive microorganism much less microorganisms of the genus *Staphylococcus* or *Enterococcus*. The pharmaceutical compositions used in the claimed method would not provide treatment or prevention against any gram-positive bacteria. The specification has not provided enablement for the claimed method since there are no working examples in the instant specification that demonstrate effectiveness of the peptide against all gram-positive microbial infections .nor has the instant specification enabled the use of mutacin I to treat or prevent infections caused by microorganisms of the genera *Staphylococcus* or *Enterococcus*. One skilled in the art would have to possess the knowledge or be provided with sufficient guidance to determine if the pharmaceutical compositions would reach the target microorganisms in order to treat or prevent infection.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or

guidance is presented in the specification with respect using the amino acid sequence as set forth in SEQ ID NO:2 to treat or prevent all gram-positive infections, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). It would require undue experimentation by one of skill in the art to determine whether the pharmaceutical compositions used in the claimed method would be effective in treating or preventing any gram-positive microbial infection or disease. One of skill in the art would require guidance, in order to practice the claimed invention in a manner reasonable in correlation with the claims. Without proper guidance, the experimentation is undue.

II. Claims 9-10 are rejected under 35 U.S.C. 102(b) as anticipated by Ikeda et al *(Infection and Immunity, 1982, Vol. 35, No. 3, p. 861-868).*

Claims 9-10 are directed to a method of treating or preventing an infection in a subject said method comprising administering to said subject an effective amount of a purified and isolated peptide having the amino acid sequence as set forth in SEQ ID NO: 2 or a pharmaceutical acceptable salt, amide, ester or prodrug thereof.

Ikeda et al teach a method of treating rats against infection caused by *Streptococcus mutans* by administering mutacin in the drinking water and the diet of these animals (see the Abstract and page 863). Ikeda et al teach that when water or diet containing the bacteriocin from Streptococcus mutans was administered to animals the caries score of these animals was found to be significantly reduced (see the

Abstract). The amino acid sequence as set forth in SEQ ID NO: 2 would be inherent in the teachings of the prior art. Ikeda et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

III. Claims 9-10 are rejected under 35 U.S.C. 102(b) as anticipated by Ooshima et al *(Microbiol. Immunol., Vol. 29 (12), 1163-1173, 1985).*

Claims 9-10 are directed to a method of treating or preventing an infection in a subject said method comprising administering to said subject an effective amount of a purified and isolated peptide having the amino acid sequence as set forth in SEQ ID NO: 2 or a pharmaceutical acceptable salt, amide, ester or prodrug thereof.

Ooshima et al teach a method of treating rats against infection caused by *Streptococcus mutans* by administering mutacin in the drinking water and the diet of these animals (see the Abstract and page 863). Ooshima et al teach that when water or diet containing the bacteriocin from Streptococcus mutans was administered to animals the dental caries of these animals was found to be significantly reduced (see the Abstract). The amino acid sequence as set forth in SEQ ID NO: 2 would be inherent in the teachings of the prior art. Ooshima et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

(10) Response to Arguments

I. Response to Arguments Traversing the Rejection of claims 9-28 under 35 U.S.C .112 first paragraph enablement.

Appellants Specific Arguments Restated

A) Appellant urges that the claimed invention is fully enabled. Appellant urges the enablement rejection under review is based on cited references which describe various pathogenic bacteria and noted that the present specification does not specifically include information regarding these bacteria. Appellant urges that the instant specification states "that mutacin I has advantages compared to conventional antimicrobial agents and it has a wide spectrum of antimicrobial activity against a wide range of gram-positive bacteria including the multidrug resistant Staphylococci and Enterococci..." (page 18 specification). The instant specification states that "mutacin III is more potent than mutacin I against *Staphylococcus aureus* and *Staphylococcus epidermidis* while both mutacins have equal activities against other pathogens such as

enterococci, pneumoncocci and Group A streptococci (page 33). Appellant urges that they have made of record the Declaration by an inventor, Dr. Page Caufield (Appendix B) including data showing particular gram-positive organisms' response to the action of mutacin I and supporting the disclosure of a wide spectrum of antimicrobial activity against a wide range of gram-positive bacteria including the multidrug resistant Staphylococci and Enterococci. Appellant submits that the Declaration supports the assertion that undue experimentation is not required to make and use the methods of the present claims an is entitled to proper weight of consideration.

B) Appellant submits that testing the susceptibility of a particular microorganism to an inventive peptide is well within the talents of one of skill in the art as evidenced by published results. in support of their position, Appellant refers to the Loyola-Rodriguez reference for an exemplary teaching with respect to table 2 of methodologies for measuring the level of success. In support of their position Appellant mad of record, A.J. Clinical Pathol., 60:384-394, 1973).

II. Response to Arguments Traversing the Rejection of claims 9-10 are rejected under 35 U.S.C. 102(b) as anticipated by Ikeda et al *(Infection and Immunity, 1982, Vol. 35, No. 3, p. 861-868).*

Appellant urges that Ikeda et al cannot be used as an anticipatory reference. Applicant urges the protein of Ikeda et al is bacteriocin C3603 isolated from the culture supernant of *Streptococcus mutans.* Appellant urges that the C3603 is not

equivalent to the protein of SEQ ID NO:2 because the molecular weight of C3603 is 4800 daltons. Appellant asserts that C3603 contains different amino acids than the protein as set forth SEQ ID NO:2.

Appellant urges that Ikeda et al include the information that "bacteriocin C3603 contains aspartic acid, threonine, serine, glutamic acid, glycine, alanine, valine, methionine, isoleucine, tyrosine, phenylalanine, tryptophan, lysine and arginine. Appellant urges that the instant specification shows that the protein of Ikeda et al could not contain the protein of SEQ ID NO:2 without also containing the amino acids leucine, cysteine, asparagine and proline. Appellant urges that the reference must teach each and every element of the claim and the reference is not directly or under the doctrine of inherency.

III. Response to Arguments Traversing the Rejection of claims 9-10 are rejected under 35 U.S.C. 102(b) as anticipated by Ooshima et al *(Microbiol. Immunol., Vol. 29 (12), 1163-1173, 1985).*

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Appellant urges that Ikeda et al include the information that "bacteriocin C3603 contains aspartic acid, threonine, serine, glutamic acid, glycine, alanine, valine, methionine, isoleucine, tyrosine, phenylalanine, tryptophan, lysine and arginine. Appellant urges that the instant specification shows that the protein of Ikeda et al could not contain the protein of SEQ ID NO:2 without also containing the amino acids leucine, cysteine, asparagine and proline. Appellant urges that the reference must teach each and every element of the claim and the reference is not directly or under the doctrine of inherency.

Examiner's Response to Appellant's Arguments

I. Applicant's arguments filed December 21, 2007 have been fully considered but they are not persuasive.

A) It is the Examiner's position that the claimed invention is not enabled by the instant specification. It should be remembered that independent claim 9 encompasses all gram-positive bacteria. The instant specification has not provided enablement to treat or prevent all gram-positive bacteria infections. Pages 12-21 of the instant specification does not enable the treatment or prevention of all gram-positive infections using mutacin I. The instant specification has not provided any experimental examples to demonstrate that the claimed method can be used to treat or prevent all gram-positive bacteria. The instant specification merely makes the statement the "…. Mutacin III is more potent than mutacin I against *S. aureus* and *S. epidermidis* while both mutacins have equal activities against other pathogens such as enterococci,

pneumococci and Group A streptococci" (page 33). It is noted that pathogens such as enterococci, pneumococci and Group A streptococci are *only* a few microorganisms within the broad genus of *all* gram-positive bacteria. The prior art cites microorganisms from the genera *Clostridium*, *Bacillus* and *Listeria* to indicated that the claimed genus of all gram-positive microorganisms is a *very broad genus*. It should be noted that the claims also recite "prevention of gram-positive infection". It should be remembered that the term "prevention" or "preventing" encompasses the ability of the specific antigen to induce protective immunity to all gram-positive infection or disease induction. The specification does not provide substantive evidence that the peptides used in the claimed method are capable of inducing protective immunity. This demonstration is required for the skilled artisan to be able to use the claimed method for its intended purpose of preventing all gram-positive infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the peptides used in the claimed, i.e. would not be able to accurately predict if protective immunity has been induced.

The Declaration submitted by Dr. Caufield is insufficient to overcome this rejection. The Declaration submitted by Dr. Caufield, discloses inhibition that assays (*in vitro* assays) were preformed using, *S. pyogenes, S. pneumoniae*, multiple drug resistant *Staphylococcus aureus*, vancomycin –resistant *E. faecium* and *Bacillus anthracis*. It should be noted that Appendix A, submitted with the declaration, lacks clarity since the photocopies of the results of inhibition assays are unclear. However, this declaration only encompasses a few species within *the Staphylococcus,*

Streptococcus, Enterococcus and *Bacillus* genera and not all species or strains within these genera as encompassed by claim 17. Nor does the data submitted in the declaration include all gram-positive bacteria as encompassed by claim 9.

The Declaration submitted by Dr. Caufield has failed to provide a correlation between *in vitro* studies and what would be demonstrated *in vivo*. The declaration as well as the instant specification has failed to teach or disclose a method of treating or preventing gram-positive infection in a subject (*in vivo*) by administering mutacin I (SEQ ID NO:2) and then challenging the subject to see what level of protection (preventing) or treatment can be obtained. Preventing or treating gram positive infections in a subject is a requirement of the claimed method. Without this demonstration, Appellant has not met his burden under 35 U.S.C. 112, first paragraph.

B) To address Appellant's arguments regarding testing the susceptibility of a particular microorganism to an inventive peptide (e.g. references to Loyola-Rodriguez et al or A.J. Clinical Pathol., 60:384-394, 1973), it should be remembered that 112 first paragraph requires that the instant specification teach how to "make and use" the claimed invention and not "how to find out how to use the claimed method". Although it is known in the art to test or measure the success of inventive peptide, i.e. administration of SEQ ID NO:2, the instant specification has not demonstrated that the peptide set forth in SEQ ID NO:2 is effective in treating and preventing all gram-positive bacterial infections. It is the Examiner's position that it would require undue experimentation to practice (make and use) the claimed invention based on the teachings of the instant specification.

II. Applicant's arguments filed December 21, 2007 have been fully considered but they are not persuasive.

It should be remembered that comprising or open claim language means that other components can be contained in a composition. It should be remembered that the claims recite open-ended claim language, i.e. "comprising". It should be remembered that the MPEP 2111.03:

> The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Invitrogen Corp. v. Biocrest Mfg., L.P., 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) ("The transition comprising' in a method claim indicates that the claim is open-ended and allows for additional steps.");< Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts").

Thus, the claims are not limited to SEQ ID NO:2. Therefore, a protein can be larger than SEQ ID NO:2 or can be comprised within a molecule that has higher molecule weight than SEQ ID NO:2 (e.g. the weight of C3603) used in the claimed method reads on the claimed invention. Further, the pending claims do not recite a specific molecular weight for SEQ ID NO:2.

As stated above, Ikeda et al teach a method of treating rats against infection (dental caries) caused by *Streptococcus mutans* by administering mutacin in the drinking water and the diet of these animals (see the Abstract). Applicant has not provided evidence that the protein used in the claimed method is not the same as the

protein used in the method of the prior art. Thus, since the protein (a antimicrobial bacteriocin) of the prior art used in a method of treating dental caries (e.g. a method of treating a gram-positive bacterial infection) reads on the claimed invention.

To address Appellant's comments regarding content of the protein (e.g. amino acids), it should be noted that both the claimed protein as set forth in SEQ ID NO: 2 and the bacteriocin of the prior art both comprises the amino acids threonine, serine, glycine, valine, tyrosine and phenylalanine. It should be noted that the bacteriocin of the prior art comprises aspartic acid, glutamic acid, alanine, methionine, isoleucine, tryptophan, lysine and arginine and these amino acids are comprised in SEQ ID NO:2. However, it should be noted that the claims are not limited to SEQ ID NO:2 and since the claims recited "comprising" or "open claim language" the additional amino acids comprised in the bacteriocin of the prior art does not mean that the protein as set forth in SEQ ID NO:2 is not inherently present in the bacteriocin of the prior art.

In view of the above this rejection is maintained.

III. Applicant's arguments filed December 21, 2007 have been fully considered but they are not persuasive.

It should be remembered that comprising or open claim language means that other components can be contained in a composition. It should be remembered that the claims recite open-ended claim language, i.e. "comprising". It should be remembered that the MPEP 2111.03:

The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude

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Thus, the claims are not limited to SEQ ID NO:2. Therefore, a protein can be larger than SEQ ID NO:2 or can be comprised within a molecule that has higher molecule weight than SEQ ID NO:2 (e.g. the weight of C3603) used in the claimed method reads on the claimed invention. Further, the pending claims do not recite a specific molecular weight for SEQ ID NO:2.

As stated above, Ooshima et al teach a method of treating animals against infection (dental caries) caused by *Streptococcus mutans* by administering mutacin in the drinking water and the diet of these animals (see the Abstract). Appellant has not provided evidence that the protein used in the claimed method is not the same as the protein used in the method of the prior art. Thus, since the protein (a antimicrobial bacteriocin) of the prior art used in a method of treating dental caries (e.g. a method of treating a gram-positive bacterial infection) reads on the claimed invention.

To address Appellant's comments regarding content of the protein (e.g. amino acids), it should be noted that both the claimed protein as set forth in SEQ ID NO: 2 and the bacteriocin of the prior art both comprises the amino acids threonine, serine, glycine, valine, tyrosine and phenylalanine. It should be noted that the bacteriocin of

the prior art comprises aspartic acid, glutamic acid, alanine, methionine, isoleucine, tryptophan, lysine and arginine and these amino acids are comprised in SEQ ID NO:2. However, it should be noted that the claims are not limited to SEQ ID NO:2 and since the claims recited "comprising" or "open claim language" the additional amino acids comprised in the bacteriocin of the prior art does not mean that the protein as set forth in SEQ ID NO:2 is not inherently present in the bacteriocin of the prior art.

In view of the above this rejection is maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

Examiner's Answer Conclusion

For the above reasons, it is believed Examiner should be affirmed.

Respectfully submitted,

/Vanessa L. Ford/

Examiner, Art Unit 1645

March 29, 2008

Conferees

/Shanon A. Foley/
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